

REMARKS

Claims 1-38 were pending the application. Claims 1-7, 20, 21, 23, 24, 35, 36, 37, and 38 have been amended. Accordingly, upon entry of this amendment, claims 1-38 will remain pending. For the Examiner's convenience, the pending claims are set forth in Appendix A.

Support for the amendments to claims 1-7, 20, 21, 23, 24, 35, 36, 37, and 38 may be found throughout the specification, including the originally filed claims.

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the subject matter of Applicants' invention in order to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Sequence Rules Compliance

In the instant Office Action, the Examiner has required that amendments reciting SEQ ID NOs be made to the instant application. In particular, The Examiner is of the opinion that

[t]his application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 (d), as follows. Where the description or claims of a patent application discuss a sequence that is set forth in the Sequence Listing in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by SEQ ID NO: in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

The Examiner is further of the opinion that

The Sequence Listing properly lists sequences identified by SEQ ID NO's; however, the sequences disclosed in the specification and recited in the claims are not identified by SEQ ID NO's corresponding to those of the Sequence Listing. For example, Appendices A and B disclose nucleic acid

and amino acids sequences not identified by SEQ ID NO's. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicants have amended the claims to recite specific SEQ ID NOs. as required by the Examiner. *Applicants respectfully submit that since the claims, as amended, refer to specific SEQ ID NOs which are contained within the Sequence Listing, the sequences listed in Appendices A and B are not critical in determining patentability of the claims.* Moreover, Applicants respectfully submit that Appendices A and B contain nucleotide and amino acid sequences which correspond exactly with sequences contained within in the Sequence Listing. Each and every sequence listed in Appendices A and B is annotated by a specific reference number (e.g., RXA00005). These reference numbers are contained within the Sequence Listing itself, and are used to identify each of the corresponding sequences contained in Appendices A and B. Accordingly, Applicants respectfully submit that the instant application complies with the requirements of 37 C.F.R. §1.821(d) and request that the Examiner withdraw the instant objection.

CONCLUSION

In view of the amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE**In the Claims:**

Claims 1-7, 20, 21, 23, 24, 35, 36, 37, and 38 have been amended as follows:

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or a complement thereof ~~from *Corynebacterium glutamicum* encoding an SES protein, or a portion thereof,~~ provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.

2. (Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleic acid molecule encodes an SES ~~protein~~ polypeptide involved in the production of a fine chemical.

3. (Amended) An isolated *Corynebacterium glutamicum* nucleic acid molecule ~~selected from the group consisting of those sequences set forth in Appendix A, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1~~ comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

4. (Amended) An isolated nucleic acid molecule which encodes a polypeptide ~~sequence selected from the group consisting of those sequences set forth in Appendix B, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1~~ comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24.

5. (Amended) An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a *Corynebacterium glutamicum* polypeptide ~~selected from the group of amino acid sequences consisting of those sequences set forth in Appendix B, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1~~ comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or

SEQ ID NO:24, wherein the nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23 in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

6. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence which ~~is at least 50% homologous to~~ has at least 50% identity with the a nucleotide sequence ~~selected from the group consisting of those sequences set forth in Appendix A, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1~~ of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

7. (Amended) An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of ~~a nucleic acid comprising a~~ the nucleotide sequence of ~~selected from the group consisting of those sequences set forth in Appendix A, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1~~ SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

20. (Amended) An isolated polypeptide comprising ~~an~~ the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24 ~~selected from the group consisting of those sequences set forth in Appendix B, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.~~

21. (Amended) An isolated polypeptide comprising a naturally occurring allelic variant of a polypeptide comprising ~~an~~ the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24 ~~selected from the group consisting of those sequences set forth in Appendix B, or a portion thereof, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.~~

23. (Amended) An isolated polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which ~~is at least 50% homologous to a nucleic acid~~ has at least 50% identity with the nucleotide sequence ~~selected from the group consisting of~~ SEQ

ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof ~~those sequences set forth in Appendix A, provided that the nucleic acid molecule does not consist of any of the F-designated nucleic acid molecules set forth in Table 1.~~

24. (Amended) An isolated polypeptide comprising an amino acid sequence which ~~is at least 50% homologous to an~~ has at least 50% identity with the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24 ~~selected from the group consisting of those sequences set forth in Appendix B, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.~~

35. (Amended) A method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject, comprising detecting the presence of one or more of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof ~~the sequences set forth in Appendix A or Appendix B in the subject, provided that the sequences are not or are not encoded by any of the F-designated sequences set forth in Table 1,~~ thereby diagnosing the presence or activity of *Corynebacterium diphtheriae* in the subject.

36. (Amended) A host cell comprising ~~a~~ the nucleic acid molecule of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof ~~selected from the group consisting of the nucleic acid molecules set forth in Appendix A,~~ wherein the nucleic acid molecule is disrupted.

37. (Amended) A host cell comprising ~~a~~ the nucleic acid molecule of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof ~~selected from the group consisting of the nucleic acid molecules set forth in Appendix A,~~ wherein the nucleic acid molecule comprises one or more nucleic acid modifications ~~from the sequence set forth in Appendix A.~~

38. (Amended) A host cell comprising ~~a~~ the nucleic acid molecule of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof ~~selected~~

~~from the group consisting of the nucleic acid molecules set forth in Appendix A,~~ wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.

APPENDIX A

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or a complement thereof.
2. The isolated nucleic acid molecule of claim 1, wherein said nucleic acid molecule encodes an SES polypeptide involved in the production of a fine chemical.
3. An isolated *Corynebacterium glutamicum* nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.
4. An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24.
5. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a *Corynebacterium glutamicum* polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24, wherein the nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23 in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.
6. An isolated nucleic acid molecule comprising a nucleotide sequence which has at least 50% identity with the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.
7. An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

8. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1-7 under stringent conditions.
9. An isolated nucleic acid molecule comprising the nucleic acid molecule of claim 1 or a portion thereof and a nucleotide sequence encoding a heterologous polypeptide.
10. A vector comprising the nucleic acid molecule of claim 1.
11. The vector of claim 10, which is an expression vector.
12. A host cell transfected with the expression vector of claim 11.
13. The host cell of claim 12, wherein said cell is a microorganism.
14. The host cell of claim 13, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.
15. The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the modulation in production of a fine chemical from said cell.
16. The host cell of claim 15, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.
17. A method of producing a polypeptide comprising culturing the host cell of claim 12 in an appropriate culture medium to, thereby, produce the polypeptide.
18. An isolated SES polypeptide from *Corynebacterium glutamicum*, or a portion thereof.
19. The polypeptide of claim 18, wherein said polypeptide is involved in the production of a fine chemical production.

20. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24.

21. An isolated polypeptide comprising a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24.

22. The isolated polypeptide of claim 18, further comprising heterologous amino acid sequences.

23. An isolated polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which has at least 50% identity with the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

24. An isolated polypeptide comprising an amino acid sequence which has at least 50% identity with the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, or SEQ ID NO:24.

25. A method for producing a fine chemical, comprising culturing a cell containing a vector of claim 12 such that the fine chemical is produced.

26. The method of claim 25, wherein said method further comprises the step of recovering the fine chemical from said culture.

27. The method of claim 25, wherein said method further comprises the step of transfecting said cell with the vector of claim 11 to result in a cell containing said vector.

28. The method of claim 25, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.

29. The method of claim 25, wherein said cell is selected from the group consisting of: *Corynebacterium glutamicum*, *Corynebacterium herculis*, *Corynebacterium lilium*,

Corynebacterium acetoacidophilum, *Corynebacterium acetoglutamicum*, *Corynebacterium acetophilum*, *Corynebacterium ammoniagenes*, *Corynebacterium fujiokense*, *Corynebacterium nitrilophilus*, *Brevibacterium ammoniagenes*, *Brevibacterium butanicum*, *Brevibacterium divaricatum*, *Brevibacterium flavum*, *Brevibacterium healii*, *Brevibacterium ketoglutamicum*, *Brevibacterium ketosoreductum*, *Brevibacterium lactofermentum*, *Brevibacterium linens*, *Brevibacterium paraffinolyticum*, and those strains set forth in Table 3.

30. The method of claim 25, wherein expression of the nucleic acid molecule from said vector results in modulation of production of said fine chemical.

31. The method of claim 25, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

32. The method of claim 25, wherein said fine chemical is an amino acid.

33. The method of claim 32, wherein said amino acid is drawn from the group consisting of: lysine, glutamate, glutamine, alanine, aspartate, glycine, serine, threonine, methionine, cysteine, valine, leucine, isoleucine, arginine, proline, histidine, tyrosine, phenylalanine, and tryptophan.

34. A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1-9.

35. A method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject, comprising detecting the presence of one or more of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof, thereby diagnosing the presence or activity of *Corynebacterium diphtheriae* in the subject.

36. A host cell comprising the nucleic acid molecule of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof, wherein the nucleic acid molecule is disrupted.

37. A host cell comprising the nucleic acid molecule of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof, wherein the nucleic acid molecule comprises one or more nucleic acid modifications.

38. A host cell comprising the nucleic acid molecule of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof, wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.